

PREDOMINANCE OF RIGHT HEMISPHERE IN POST-ISCHEMIC STROKE IMMUNITY MODULATION

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ABSTRACT

Post-ischaemic stroke infectious complications are commonly found. However, the post-stroke reduction of immunity modulation has never been clearly disclosed. This study, which was aimed to disclose immunomodulation mechanism of post-ischaemic stroke, was undertaken using cross-sectional observational method to patients aged 50-60 years with ischaemic stroke in left and right cerebral hemispheres, who were compared with healthy individuals. Analysis unit was blood from cubital veins taken 7 days after the first stroke attack. Immunity status observation was carried out by measuring total lymphocytes, monocytes, IL-10, IFN- γ , and TNF- β 1. The analysis of immunity status in those three groups was done using multivariate approach. Results of Manova analysis revealed that immunity status in those groups had significant difference (Wilk's Lambda, $p < 0.05$). Furthermore, discriminant analysis performed to obtain variable that had predominant contribution to immune response revealed the following results: (1) in group with ischaemic stroke in right hemisphere, a number of discriminant variable were monocytes, IL-10, IFN- γ , and TNF- β 1, (2) in group with ischaemic stroke in left hemisphere, the discriminant variable were monocytes and IFN- γ . In conclusion, (1) ischaemic stroke, either in left and right hemispheres, induces different immunity modulation, (2) ischaemic stroke modulation in right hemisphere is contributed particularly by the role of monocytes IL-10, IFN- γ , and TNF- β 1, while that in left hemisphere by only the role of monocytes and IFN- γ . The role of IFN- γ , IL-10 on the cell immunocompetence (monocyte) is psychoneuroimmunological approach. Based on those findings, it can be seen that the function of left hemisphere may be more predominant in complementary mechanism to maintain immunological defense of the body.

Keywords: ischaemic stroke, right hemisphere, left hemisphere, immunity

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INTRODUCTION

Management of ischemic stroke often bring complications, among others, pneumonia, urinary tract infection and decubital ulcer (Lamsudin 1998). Ischemic stroke associated with infection has been examined in two perspectives. First, the complications of infection can occur in post-ischemic stroke. Second, infectious complications of ischemic stroke are seen as the cause of repeated attacks of ischemic stroke (Grau 1995, Bova 1996, Paganini 2003). Impaired Central Nervous System (CNS) causes immune modulation. It is known that disturbances in neuron, astrocyte, and microglia can cause immune modulation. Some research indicates that post-acute attack may lead to ischemic neurons. In acute attacks the body's immune decline (Tarkowski 1995). The mechanism of immune modulation involves various mediators cytokines, hormones, and polypeptide (Stenberg 1997). The results showed that IL-1 β , IL10, and IL-8 have proven to be a predictor in the modulation of immunity due to

hypoxia (Suroto 2001, Hartanto 2003). Fluctuation of IL-1 β , IL10, and IL-8 on the condition of brain tissue hypoxia will be used as a basis for the observation of immune modulation by psychoneuroimmunological approach.

MATERIALS AND METHODS

The design of this study was observational-sectional. The population was all patients with ischemic stroke that hospitalized at Dr. Moewardi Surakarta in May-July 2003. The sample was part of the population of ischemic stroke patients with the following sample criteria: age 50-60 years, the first stroke, the CT scan showed an ischemic stroke both left and right hemispheres, erythrocytes and hemoglobin within normal limits, random blood sugar within normal limits, liver function within normal limits, renal function within normal limits. All patients who meet the criteria of the sample followed for 7 days post-stroke.

Total lymphocytes and monocytes examined by means of cell dyn 3300. IL-10, IFN- γ , TGF- β 1 were measured by using enzyme-linked immunosorbent assay (ELISA). The data were analyzed with statistical tests at significance level 0.05. Homogeneity test conducted on moderator variables to see the physical condition and health of the sample in the same condition. To test IIDN dependent variable (Identically Independence and normality) to see the variety and independence of the data of each group. Manova test performed on different immunity between the stroke right or left to control. Discriminant analysis is used to help get a response as distinguishing variables that have a strong contribution to the biological process of immune modulation.

RESULTS

Samples that can be used to support the existence of an ischemic stroke includes ischemic area (SIH left = 0.61

± 0.10 , SIH right = 0.63 ± 0.08) and cholesterol control = 2008 ± 8.7 , left = 206 ± 8.4 , SIH right = 206.7 ± 8.3 by t test there is no difference, while the systolic pressure in all groups of 115-140 mmHg and diastolic 70-85 mmHg. All variables obtained homogeneous ($p > 0.05$) and within normal limits.

Manova test results between groups differences between the control group, the left hemisphere and right hemisphere difference found between groups (Wilk's Lambda, $p < 0.05$), so the immune status of the three groups showed differences. The result of discriminant analysis right hemisphere ischemic stroke group with the control variables obtained differentiating monocytes, IL-10, IFN- γ , TGF- β 1. The result of discriminant analysis of the left hemisphere ischemic stroke group with the control variables obtained differentiating monocytes and IFN- γ .

Table 1 Mean and Standard Deviation

Groups	Variables				
	Lymphocytes ($10^3/\mu\text{L}$)	Monocytes ($10^3/\mu\text{L}$)	IFN- γ (pg/ml)	IL-10 (pg/ml)	TGF- β 1 (pg/ml)
Control	2.4115	0.52290	0.8440	0.7710	59.8375
	± 0.5153	± 0.16803	± 1.9826	± 0.9911	± 18.2044
Right hemisphere	2.1244	0.70589	4.7300	3.9489	36.3756
	± 0.8829	± 0.18822	± 3.6273	± 1.8403	± 10.6810
Left hemisphere	2.0400	0.73800	5.3500	2.3170	42.8890
	± 0.5731	± 0.18900	± 4.6495	± 1.9360	± 22.9741

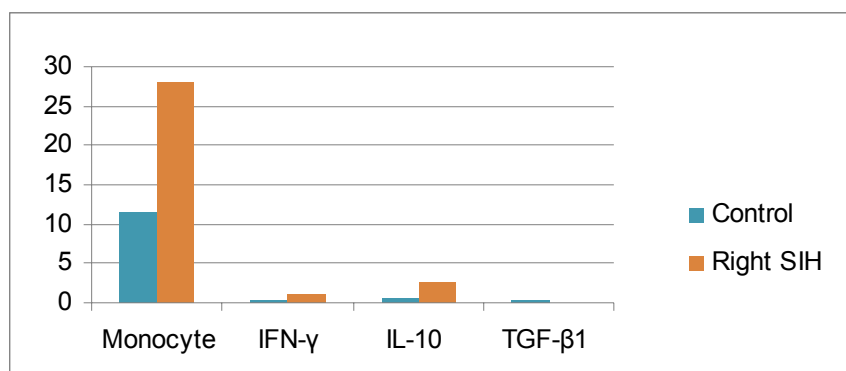


Figure 1. Immunity pattern of right SIH and control.

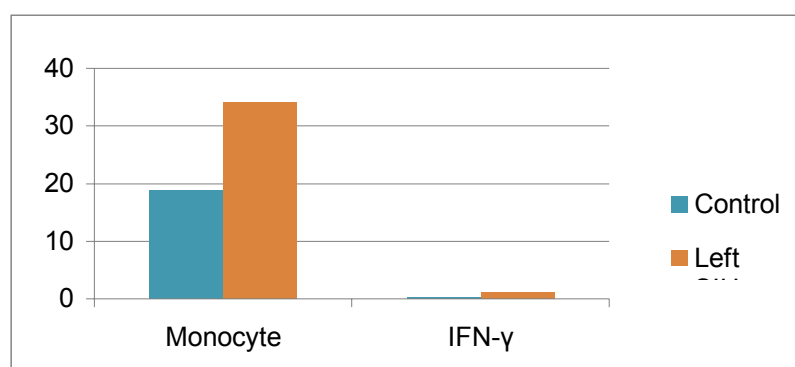


Figure 2. Immunity pattern of left SIH and control.

On the right SIH immunity pattern was found that increasing the contribution of monocytes is modulated by the role of IFN- γ and IL-10, whereas the role of TGF- β . A decline. On the left SIH immunity pattern was found that increasing the contribution of monocytes is modulated only by the role of IFN- γ . Thus the pattern of modulation of immunity seven days after ischemic stroke between left hemisphere and right hemisphere difference was found.

DISCUSSION

All three groups showed differences in immunity and all three showed modulation of immunity. Based on the average of the dependent variables showed that in ischemic stroke shows (1) the number of peripheral lymphocytes and TGF- β . There is a decrease and (2) the number of peripheral blood monocytes, IFN- γ , and IL-10 increases. On the basis of the results of measurements above the mean of these variables, the ischemic condition can cause inflammation, especially the marked increase in IFN- γ . Increased levels of IFN- γ in modulation of the amount of possible blood monocyte phagocytic blood as a candidate on the network. Tarkowski (1995) have obtained a decrease of lymphocytes in the condition of stroke. Impairment of TGF- β 1 reflects Th3 negative role in the modulation of inflammation (Suroto 2001). Rabin (1989) and Owens-Babcock (2002) states that the central nervous system and immune system has a modulation in both directions. Stress conditions in both systems will mutually affect the activities of various cells in the system. Tarkowski (1995) found that ischemic stroke can cause modulation lateralization of the delayed-type hypersensitivity (DTH) or DTH responses obtained are asymmetric between the right hemisphere ischemic stroke and left hemisphere.

Based on the amount of the contribution of variables in a pattern of acquired immunity ischemic stroke right role monocytes, IFN- γ , and IL-10 in the immune status of prominent, especially on monocytes. This phenomenon is caused by the modulation of IFN- γ can increase monocyte differentiation and vice versa can also trigger monocytes to secrete IFN- γ (Goldsby 2000, Schroder 2003). Increased secretion of IFN- γ and IL-10 can also be made possible by the autocrine effects of IFN- γ and IL-10 on astrocyte and microglia, because both these cells also have receptors have both these cytokines (Stenberg 1997, Vitkovic 2000). On the basis of these autocrine effect on the condition that is still in a period of inflammation, the astrocyte and microglia experiencing excessive stress to secrete autocrine.

The pattern of left hemisphere ischemic stroke immunity only showed increased immune response sufficient contribution of the role of IFN- γ and monocytes. However, the role of IL-10 is less dominant so that the left hemisphere ischemic stroke stressors do not include modulation broader immunocompetent cells. In the right hemisphere ischemic stroke have reflected immune modulation compensation greater than the left hemisphere ischemic stroke. Left brain hemisphere is more involved in "thinking", "social being", and biological emotions, so that the right hemisphere ischemic stroke is possible for the independence of psychomotor function and social function of patients is still good, and the quantity of post-stroke stressors is lower.

CONCLUSION

Post-ischemic right hemisphere stroke and left hemisphere obtained different immune modulation. Immune modulation after ischemic stroke is more

dominant right hemisphere (monocytes, IL-10, IFN- γ , and TGF- β 1) compared with left hemisphere ischemic stroke (monocytes and IFN- γ). This is possibly due to complementation left brain function in maintaining immune homeostasis in ischemic stroke right hemisphere is more dominant.

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